

# Myocardial infarction centres: the way forward

H R Andersen, C J Terkelsen, L Thuesen, L R Krusell, S D Kristensen, H E Bøtker, J F Lassen, T T Nielsen

*Heart* 2005;91(Suppl III):iii12–iii15. doi: 10.1136/hrt.2004.058537

In the era of primary PCI, a strategy of admitting patients to the nearest hospital should be obsolete. Instead, a pre-hospital diagnostic strategy should be implemented in order to: (1) refer patients directly to interventional centres, thereby eliminating delay at local hospitals; (2) alert the interventional centre, thereby reducing door to balloon times; (3) initiate adjunctive medication in the prehospital phase

Patients with ST elevation myocardial infarction (STEMI) constitute approximately half of all patients who are admitted with acute myocardial infarction (AMI).<sup>1</sup> In these patients reperfusion treatment, either thrombolysis or primary percutaneous coronary intervention (PCI), should be initiated as soon as possible to ensure optimal patient outcome.<sup>2–3</sup>

Major disadvantages of thrombolysis are: 30–60 minutes may elapse from hospital admission until initiation of treatment (unless prehospital thrombolysis is an option); additional 30–60 minutes elapse until reperfusion is achieved (if achieved at all); and patients are at increased risk of reinfarctions and strokes when compared with an interventional treatment strategy.<sup>4–5</sup>

The major disadvantage of primary PCI is admission of the majority of patients to hospitals without interventional facilities. In these patients acute transfer to an interventional centre is required causing further delay in initiation of the treatment. Nonetheless, recent trials have documented that a strategy of emergent interhospital transfer is not only feasible and safe but also associated with improved clinical outcome.<sup>4–10</sup>

## TIME DEPENDENT PROGNOSTIC BENEFIT OF REPERFUSION TREATMENT

It has been claimed that the time dependent prognostic benefit of thrombolysis cannot be copied to primary PCI, if treatment delay (time from symptom onset until initiation of reperfusion treatment) is below 2–3 hours.<sup>11–13</sup> This is in contrast to trials documenting that long door to balloon times (time from hospital admission until first balloon inflation) and long symptom onset to balloon times, respectively, are associated with increased mortality.<sup>14–15</sup> Furthermore, a recent study has shown that each additional 30 minute delay in the initiation of treatment with primary PCI is associated with a 7.5% increased risk of dying.<sup>16</sup> Therefore, we should try to reduce treatment delays further in the setting of primary PCI.

In the following, we describe requirements for an optimal regional strategy of primary PCI, which may result in a substantial reduction of treatment delays.

## REQUIREMENTS FOR A SUCCESSFUL REGIONAL STRATEGY OF PRIMARY PCI

In the era of thrombolysis, reperfusion treatment was available even at the smallest hospital and in some cases in

the prehospital phase. Outcome was independent of hospital volume. Neither of these are the case in primary PCI.<sup>17–18</sup> Due to volume dependent success rates primary PCI should be considered as an acute reperfusion treatment only at hospitals where the volume of procedures is sufficiently large for physicians to develop and maintain their skills. Accordingly, the American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend that PCI for AMI should only be performed in high volume centres (> 400 procedures/year) with fully equipped interventional laboratories available on a 24 hour basis.<sup>19</sup> Thus, in regions where a high volume primary PCI centre can be reached within two hours from patient contact to the medical system, primary PCI should be the preferred treatment.<sup>4</sup> This calls for a reorganisation of the current regional strategy in order to treat all patients living within two hours of transport time from the interventional centre with primary PCI.

The first requirement to achieve a successful regional strategy for primary PCI is an agreement among all cardiologists in the region upon an interventional treatment strategy. Subsequently, a high volume centre with 24 hour interventional capabilities should be established, and all non-interventional hospitals located within two hours of transport should be identified. A “trauma team approach” to patients with STEMI should be established in the region in close collaboration between the emergency medical system, the local hospitals, and the interventional centre.

## OPTIMAL PREHOSPITAL STRATEGY

Patient delay (time from onset of symptoms until calling for help) is still the major contributor of treatment delay (time from onset of symptoms until initiation of reperfusion treatment). Media campaigns have failed to yield a long lasting reduction in patient delay.<sup>20–21</sup> Still, we should encourage people to call for help as soon as possible after onset of chest pain, and patients should be informed that contact to the emergency medical system is preferable. It is well documented that contact to a general practitioner prolongs the prehospital delay.<sup>22</sup> Likewise, even though self transportation results in earlier admission, it delays initiation of reperfusion treatment.<sup>23</sup> Moreover, in order to benefit from prehospital diagnosis it is mandatory that patients contact the emergency medical system when experiencing relevant cardiac symptoms.

The next step is establishment of a prehospital diagnosis. Prehospital 12 lead ECG capabilities must be available. If ambulances are neither staffed with physicians, nor with paramedics trained in prehospital diagnosis, a strategy of transmitting the ECGs to a hospital for further analysis

**Abbreviations:** AMI, acute myocardial infarction; door-to-balloon time, time from hospital admission until first balloon inflation; facilitated PCI, thrombolytic therapy followed by acute PCI; patient delay, time from onset of symptoms until calling for help; PCI, percutaneous coronary intervention; STEMI, ST elevation myocardial infarction; treatment delay, time from symptoms onset until initiation of reperfusion treatment

**Table 1** Delays in patients with acute ST elevation myocardial infarction transferred acutely from local hospitals to interventional centres for primary percutaneous coronary intervention

| Trial                   | n   | Time from arrival at local hospital to departure | Time from departure from local hospital to arrival at interventional centre | Time from arrival at interventional centre to first balloon inflation | Time from symptom onset to first balloon inflation |
|-------------------------|-----|--------------------------------------------------|-----------------------------------------------------------------------------|-----------------------------------------------------------------------|----------------------------------------------------|
| Maastricht <sup>7</sup> | 75  | NA                                               | 20†                                                                         | NA                                                                    | 230†                                               |
| PRAGUE-1 <sup>6</sup>   | 101 | 32*                                              | 35*                                                                         | 28*                                                                   | 215*                                               |
| DANAMI-2 <sup>4</sup>   | 567 | 50*                                              | 32*                                                                         | 26*                                                                   | 224*                                               |
| PRAGUE-2 <sup>7</sup>   | 429 | NA                                               | 48*                                                                         | 26*                                                                   | 277*                                               |
| Air PAMI <sup>8</sup>   | 71  | 73*                                              | 26*                                                                         | 25*                                                                   | NA                                                 |

Time in minutes: \*median; †mean.  
NA, not available.

should be implemented.<sup>24–27</sup> A default programme of transporting patients with STEMI to the nearest hospital is obsolete.<sup>11</sup> The major implication of prehospital diagnosis is referral of patients directly to the interventional centres, bypassing local hospitals. Thereby the 30–50 minute delay at local hospitals is avoided (table 1), and the total treatment delays can be shortened as much as one hour (fig 1).<sup>4–9–28</sup> However, we must ensure a safe strategy of direct referral. In some regions ambulance physicians are present. In other regions ambulance personnel are responsible for such long patient transportations, which requires a level of education that may be more extensive than at present. Alternatively a strategy of rendezvous could be implemented, implying that the ambulance staffs require a prehospital physician or nurse to meet them on the route to the interventional centre.

In patients triaged for admission directly to interventional centres, prehospital diagnosis is also relevant in order to bypass the emergency room and the coronary care unit and to alert the catheterisation laboratory before patient arrival. This may reduce door to balloon times to approximately 30 minutes,<sup>28</sup> thus considerably lower than the 100–120 minutes observed in recent large scale trials and population based registries.<sup>4–9–14</sup>

### LOCAL HOSPITAL: OPTIMAL STRATEGY

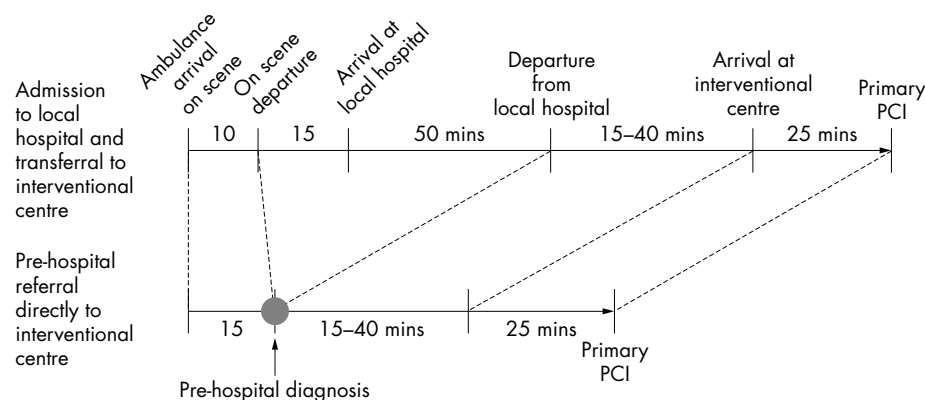
If direct referral from the scene of the event to the interventional centre is not possible, at least a strategy of emergency interhospital transfer should be implemented. In order to reduce delays at local hospitals, prehospital diagnosis should be performed. Thereby, the local hospital is alerted before patient arrival and necessary arrangements can be made for emergency interhospital transfer. In patients who present themselves to a local hospital, local heart attack units should implement a triage that ensures fast establishment of

the diagnosis and transfer to the interventional centre. The number of patients who present themselves is relatively low in most European countries (15–20%), whereas it is considerable higher in the USA (50%).

### INTERVENTIONAL CENTRE: OPTIMAL STRATEGY

Patient transfer to interventional centres should not be delayed by difficulties in communication between physicians. The local hospitals as well as the emergency medical systems (in the setting of prehospital diagnosis) should have the privilege to make the decision to transfer patients with STEMI without negotiating with the primary PCI centre. The interventional centre should be alerted before patient arrival, either by the emergency medical system (in the setting of prehospital diagnosis and direct referral to primary PCI), or by the local hospital (in the setting of acute transfer to primary PCI). This early contact allows time to prepare the cardiac catheterisation laboratory and to alert all personnel involved. The patient should be directed to the cardiac catheterisation laboratory, avoiding initial admission to the emergency department or coronary care unit. Whether alerted by the local hospital or by the emergency medical system, door to balloon times of 25–30 minutes can be achieved.<sup>4–6–8–9–28</sup>

Most patients can return to their local hospital within 12 hours of admission. If feasible and safe a strategy of “drive-in PCI” might be adopted in the future. The local hospital should function as a subunit of the regional myocardial infarction centre, allowing follow up to be maintained in the patient’s home district. Likewise, the need for further revascularisation should be coordinated in close collaboration between the cardiologists at the local hospitals and the interventional centre.

**Figure 1** Delays in initiation of primary percutaneous coronary intervention (primary PCI) among patients with acute ST elevation myocardial infarction living in catchment areas of local hospitals.

### Requirements for a successful regional interventional treatment strategy in patients with acute ST elevation myocardial infarction (STEMI):

1. Cardiologist should agree upon an interventional treatment strategy for their region
2. A high volume PCI centre with 24 hour interventional capability should be established
3. Hospitals within two hours of transport from the interventional centre should be identified
4. Local hospitals and the interventional centre should collaborate closely
5. Cardiologists and the emergency medical system should cooperate, and adapt a trauma team approach to patients with chest pain
6. Patients should be encouraged to contact the emergency medical system when experiencing chest pain, rather than self presentation to local hospitals
7. Prehospital diagnosis should be implemented and combined with direct referral of STEMI patients to the interventional centre, bypassing local hospitals
8. The interventional centre should be alerted to reduce door to balloon times
9. Patients should be returned to the local hospital as soon as possible
10. Local hospitals should constitute a subunit of the myocardial infarction centre, managing patient follow up in the patient's home district, and establishing indications for further intervention in close collaboration with the physicians at the interventional centre

### ADJUNCTIVE MEDICATION

Aspirin and heparin is mandatory in the acute phase. The prognostic benefit of these medications may very well increase if administered in the prehospital phase.<sup>29</sup> Clopidogrel should be given at a loading dose of 300–600 mg.<sup>30</sup> Glycoprotein IIb/IIIa inhibitors improve short term target vessel revascularisation when given during the catheterisation procedure.<sup>31–33</sup> It is not yet established whether the outcome of primary PCI will be further improved by prehospital administration of a glycoprotein IIb/IIIa inhibitor.<sup>34–35</sup> So far, it is unclear whether additional benefit can be achieved if thrombolysis is given before primary PCI (facilitated PCI).

### CONCLUSION

Treatment of patients with acute ST elevation myocardial infarction with primary PCI is a superior reperfusion strategy compared to on-site thrombolysis, also among patients admitted to non-interventional hospitals located within two hours of transport to an interventional centre. We should reorganise our communities in order to reduce treatment delays and optimise patient outcome further in these patients. Thus, adapting a trauma team approach, including a regional strategy of prehospital diagnosis and referral of patients directly to interventional centres, may be one of the new successes in modern cardiology.

### Authors' affiliations

H R Andersen, C J Terkelsen, L Thuesen, L R Krusell, S D Kristensen, H E Bøtker, J F Lassen, T T Nielsen, Department of Cardiology, Skejby University Hospital, Aarhus, Denmark

Correspondence to: Henning Rud Andersen, MD, Department of Cardiology B, Skejby University Hospital, DK-8200 Aarhus N, Denmark; henning.rud.andersen@iekf.au.dk

### REFERENCES

1. Steg PG, Goldberg RJ, Gore JM, et al. Baseline characteristics, management practices, and in-hospital outcomes of patients hospitalized with acute coronary syndromes in the global registry of acute coronary events (GRACE). *Am J Cardiol* 2002;**90**:358–63.
2. Van de Werf F, Ardissino D, Betriu A, et al. Management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2003;**24**:28–66.
3. Boersma E, Maas AC, Deckers JW, et al. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *Lancet* 1996;**348**:771–5.
4. Andersen HR, Nielsen TT, Rasmussen K, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. *N Engl J Med* 2003;**349**:733–42.
5. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003;**361**:13–20.
6. Widimsky P, Groch L, Zelizko M, et al. Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE study. *Eur Heart J* 2000;**21**:823–31.
7. Vermeer F, Oude Ophuis AJM, Berg EJD, et al. Prospective randomised comparison between thrombolysis, rescue PTCA, and primary PTCA in patients with extensive myocardial infarction admitted to a hospital without PTCA facilities: a safety and feasibility study. *Heart* 1999;**82**:426–31.
8. Grines CL, Westerhausen DR Jr, Grines LL, et al. A randomized trial of transfer for primary angioplasty versus on-site thrombolysis in patients with high-risk myocardial infarction: the air primary angioplasty in myocardial infarction study. *J Am Coll Cardiol* 2002;**39**:1713–9.
9. Widimsky P, Budesinsky T, Vorac D, et al. Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction: final results of the randomized national multicentre trial – PRAGUE-2. *Eur Heart J* 2003;**24**:94–104.
10. Dalby M, Bouzamondo A, Lechat P, et al. Transfer for primary angioplasty versus immediate thrombolysis in acute myocardial infarction: a meta-analysis. *Circulation* 2003;**108**:1809–14.
11. Topol EJ, Kereiakes DJ. Regionalization of care for acute ischemic heart disease: a call for specialized centers. *Circulation* 2003;**107**:1463–6.
12. Steg PG, Bonnefoy E, Chabaud S, et al. Impact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty: data from the CAPTIM randomized clinical trial. *Circulation* 2003;**108**:2851–6.
13. Zijlstra F, Patel A, Jones M, et al. Clinical characteristics and outcome of patients with early (<2 h), intermediate (2–4 h) and late (>4 h) presentation treated by primary coronary angioplasty or thrombolytic therapy for acute myocardial infarction. *Eur Heart J* 2002;**23**:550–7.
14. Cannon CP, Gibson CM, Lambrew CT, et al. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. *JAMA* 2000;**283**:2941–7.
15. De Luca G, Suryapranata H, Zijlstra F, et al. Symptom-onset-to-balloon time and mortality in patients with acute myocardial infarction treated by primary angioplasty. *J Am Coll Cardiol* 2003;**42**:991–7.
16. De Luca G, Suryapranata H, Ottervanger JP, et al. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. *Circulation* 2004;**109**:1223–5.
17. Jollis JG, Peterson ED, DeLong ER, et al. The relation between the volume of coronary angioplasty procedures at hospitals treating medicare beneficiaries and short-term mortality. *N Engl J Med* 1994;**331**:1625–9.
18. Canto JG, Every NR, Magid DJ, et al. The volume of primary angioplasty procedures and survival after acute myocardial infarction. *N Engl J Med* 2000;**342**:1573–80.
19. Smith SC, Dove JT, Jacobs AK, et al. ACC/AHA guidelines of percutaneous coronary interventions (revision of the 1993 PTCA guidelines) – executive summary. A report of the American College of Cardiology/American Heart Association task force on practice guidelines (committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty). *J Am Coll Cardiol* 2001;**37**:2215–39.
20. Blohm M, Herlitz J, Hartford M, et al. Consequences of a media campaign focusing on delay in acute myocardial infarction. *Am J Cardiol* 1992;**69**:411–3.
21. Luepker RV, Raczynski JM, Osganian S, et al. Effect of a community intervention on patient delay and emergency medical service use in acute coronary heart disease: the rapid early action for coronary treatment (REACT) trial. *JAMA* 2000;**284**:60–7.
22. Prasad N, Wright A, Hogg KJ, et al. Direct admission to the coronary care unit by the ambulance service for patients with suspected myocardial infarction. *Heart* 1997;**78**:462–4.
23. Hutchings C, Mann N, Daya M, et al. Patients with chest pain calling 9-1-1 or self-transporting to reach definitive care: which mode is quicker? *Am Heart J* 2004;**147**:35–41.
24. Grim PS, Feldman T, Martin M, et al. Cellular telephone transmission of 12-lead electrocardiograms from ambulance to hospital. *Am J Cardiol* 1987;**60**:715–20.
25. Weaver WD, Cerqueira M, Hallstrom AP, et al. Prehospital-initiated vs hospital-initiated thrombolytic therapy. *JAMA* 1993;**270**:1211–6.

- 26 **Wall T**, Albright J, Livingstone B, *et al*. Prehospital ECG transmission speeds reperfusion for patients with acute myocardial infarction. *North Carolina Med J* 2000;**61**:104–8.
- 27 **Terkelsen CJ**, Nørgaard BL, Lassen JF, *et al*. Telemedicine used for remote prehospital diagnosing in patients suspected of acute myocardial infarction. *J Intern Med* 2002;**252**:412–20.
- 28 **Terkelsen CJ**, Lassen JF, Nørgaard BL, *et al*. Reduction of treatment delay in patients with ST-elevation myocardial infarction: impact of pre-hospital diagnosis and direct referral to primary percutaneous coronary intervention. *Eur Heart J* 2005;Jan 31 (epub ahead of print).
- 29 **Zijlstra F**, Ernst N, de Boer MJ, *et al*. Influence of prehospital administration of aspirin and heparin on initial patency of the infarct-related artery in patients with acute ST elevation myocardial infarction. *J Am Coll Cardiol* 2002;**39**:1733–7.
- 30 **Lange RA**, Hillis LD. Antiplatelet therapy for ischemic heart disease. *N Engl J Med* 2004;**350**:277–80.
- 31 **Montalescot G**, Barragan P, Wittenberg O, *et al*. Platelet glycoprotein IIb/IIIa inhibition with coronary stenting for acute myocardial infarction. *N Engl J Med* 2001;**344**:1895–903.
- 32 **Stone GW**, Grines CL, Cox DA, *et al*. Comparison of angioplasty with stenting, with or without abciximab, in acute myocardial infarction. *N Engl J Med* 2002;**346**:957–66.
- 33 **Antoniucci D**, Migliorini A, Parodi G, *et al*. Abciximab-supported infarct artery stent implantation for acute myocardial infarction and long-term survival: a prospective, multicenter, randomized trial comparing infarct artery stenting plus abciximab with stenting alone. *Circulation* 2004;**109**:1704–6.
- 34 **Topol EJ**, Neumann FJ, Montalescot G. A preferred reperfusion strategy for acute myocardial infarction. *J Am Coll Cardiol* 2003;**42**:1886–9.
- 35 **Montalescot G**, Borentain M, Payot L, *et al*. Early vs late administration of glycoprotein IIb/IIIa inhibitors in primary percutaneous coronary intervention of acute ST-segment elevation myocardial infarction: a meta-analysis. *JAMA* 2004;**292**:362–6.